WHAT IS CLAIMED IS:

1. A method for diagnosing a predisposition to epilepsy, or epilepsy itself, in a subject, the method comprising the steps of:

(a) obtaining a sample from the subject;

(b) measuring a concentration of at least two kynurenine metabolites in the sample; and

(c) comparing said concentration of said at least two kynurenine metabolites in the sample to a range of values of said concentration of said at least two kynurenine metabolites for normal individuals, such that if said concentration of said at least two kynurenine metabolites in the sample lies outside of said range of values for normal individuals, epilepsy is diagnosed in the subject.

2. The method of claim 1, wherein the sample is selected from the group consisting of a physiological liquid sample and a physiological tissue sample.

3. The method of claim 2, wherein said physiological liquid sample is selected from the group consisting of a blood sample and a urine sample.

4. The method of claim 1, wherein said at least two metabolites are selected from the group consisting of TRP (tryptophan), KYN (kynurenine), 3HOKYN (3-hydroxykynurenine), AA (anthranilic acid), 3HOAA (3-hydroxyanthranilic acid), KA (kynurenic acid) and QUIN (quinolinic acid).

5. The method of claim 4, wherein said at least two kynurenine metabolites include at least one neuroprotective metabolite and at least one neurotoxic metabolite.

6. The method of claim 5, wherein said at least two kynurenine metabolites include a pair of metabolites selected from the group consisting of KA and 3HOAA, AA and 3HOAA, and KYN and 3HOKYN.

7. The method of claim 6, wherein a ratio of said concentrations of said pair of

metabolites is measured.

8. The method of claim 7, wherein said ratio is selected from the group consisting of KA / 3HOAA, (KA+AA) /3HOAA, KA / QUIN, 3HOAA / 3HOKYN, KA/3HOAAxTRP, and (KA+AA)/3HOAAxTRP.

9. The method of claim 4, wherein a concentration of each of substantially all of said kynurenine metabolites is measured.

10. The method of claim 4, wherein said concentration of said at least two metabolites is measured by HPLC.

11. The method of claim 4, wherein said concentration of said at least two metabolites is measured by fluorimetry.

12. The method of claim 4, wherein said concentration of said at least two metabolites is measured by an immunochemical assay.

13. The method of claim 5, wherein step (c) comprises the step of determining a ratio of said at least one neuroprotective metabolite and said at least one neurotoxic metabolite, and the method further comprises the steps of:

(d) measuring a concentration of an AED (anti-epileptic drug) in the sample of the subject; and

(e) correlating said concentration of said AED with said ratio of said neurotoxic metabolite and said neuroprotective metabolite to determine an efficacy of treatment with said AED.

14. The method of claim 13, wherein said ratio is selected from the group consisting of KA / 3HOAA, (KA+AA) /3HOAA, KA / QUIN, 3HOAA / 3HOKYN, KA/3HOAAxTRP, and (KA+AA)/3HOAAxTRP.

15. The method of claim 13, further comprising the step of:

(f) adjusting a treatment regimen for said AED in the subject according to said ratio of said metabolites.

16. A method for detecting a predisposition to epilepsy in a subject, the subject being substantially free of signs and symptoms of clinical epilepsy, the method comprising the steps of:

(a) obtaining a sample from the subject;

(b) measuring a concentration of at least two kynurenine metabolites, including at least one neuroprotective metabolite and at least one neurotoxic metabolite, in the sample; and

(c) comparing said concentration of said at least two kynurenine metabolites in the sample to a range of values of said concentrations of said at least two kynurenine metabolites for normal individuals, such that if said concentrations of said at least two kynurenine metabolites in the sample lie outside of said range of values for normal individuals, the predisposition to epilepsy in the subject is detected.

17. A method for determining an efficacy of treatment with an AED (antiepileptic drug) in a subject, comprising the steps of:

(a) obtaining a sample from the subject;

(b) measuring a concentration of at least two kynurenine metabolites in the sample; and

(c) comparing said concentrations to an expected range of values for individuals with diagnosed epilepsy substantially controlled by treatment with an AED, such that the efficacy of treatment with the AED in the subject is determined.

18. The method of claim 17, wherein step (c) comprises the step of determining a ratio of said at least one neuroprotective metabolite and said at least one neurotoxic metabolite, and the method further comprises the step of:

(d) comparing said ratio to an expected range of values for individuals with diagnosed epilepsy substantially controlled by treatment with an AED, such that the efficacy of treatment with the AED in the subject is determined.

19. The method of claim 18, further comprising the steps of:

(e) measuring a concentration of the AED in the sample of the subject; and

(f) correlating said concentration of the AED with said ratio to determine the efficacy of treatment with the AED in the subject.

20. The method of claim 19, further comprising the step of:

(g) adjusting a treatment regimen for the AED in the subject according to the ratios of said metabolites.

21. A diagnostic system for diagnosing of epilepsy in a subject, comprising:

(a) a sample taken from the subject; and

(b) a measurer for measuring a concentration of at least two kynurenine metabolites, including at least one neuroprotective metabolite and at least one neurotoxic metabolite, in said sample; and

(c) a correlator for correlating said concentrations of said at least two kynurenine metabolites in said sample with a range of values for said ratios of said at least two metabolites for normal individuals, such that if said ratios of said at least two metabolites in said sample lie outside of said range of values for normal individuals, diagnosis of epilepsy in the subject is detected.

22. The diagnostic system of claim 21, wherein the sample is selected from the group consisting of a physiological liquid sample or a physiological tissue sample.

23. The diagnostic system of claim 22, wherein said physiological liquid sample is selected from the group consisting of a blood sample and a urine sample.

24. The diagnostic system of claim 23, wherein said at least two metabolites are selected from the group consisting of TRP (tryptophan), KYN (kynurenine), 3HOKYN (3-hydroxykynurenine), AA (anthranilic acid), 3HOAA (3-hydroxyanthranilic acid), KA (kynurenic acid) and QUIN (quinolinic acid).

25. The diagnostic system of claim 24, wherein said at least two kynurenine metabolites include at least one neuroprotective metabolite and at least one neurotoxic metabolite.

26. The diagnostic system of claim 25, wherein said at least two kynurenine metabolites include a pair of metabolites selected from the group consisting of KA and 3HOAA, AA and 3HOAA, and KYN and 3HOKYN.

27. The diagnostic system of claim 26, wherein a ratio of said concentrations of said pair of metabolites is measured.

28. The diagnostic system of claim 27, wherein said ratio is selected from the group consisting of KA / 3HOAA, (KA+AA) /3HOAA, KA / QUIN, 3HOAA / 3HOKYN, KA/3HOAAxTRP, and (KA+AA)/3HOAAxTRP.

29. The diagnostic system of claim 28, wherein said measurer includes a HPLC.

30. The diagnostic system of claim 28, wherein said measurer includes a fluorimeter.

31. The diagnostic system of claim 28, wherein said measurer includes an immunochemical assay.

AMENDED CLAIMS

[received by the International Bureau on 30 October 1999 (30.10.99); new claims 32-51 added; remaining claims unchanged (4 pages)]

25. The diagnostic system of claim 24, wherein said at least two kynurenine metabolites include at least one neuroprotective metabolite and at least one neurotoxic metabolite.

26. The diagnostic system of claim 25, wherein said at least two kynurenine metabolites include a pair of metabolites selected from the group consisting of KA and 3HOAA, AA and 3HOAA, and KYN and 3HOKYN.

27. The diagnostic system of claim 26, wherein a ratio of said concentrations of said pair of metabolites is measured.

28. The diagnostic system of claim 27, wherein said ratio is selected from the group consisting of KA / 3HOAA, (KA+AA) /3HOAA, KA / QUIN, 3HOAA / 3HOKYN, KA/3HOAAxTRP, and (KA+AA)/3HOAAxTRP.

29. The diagnostic system of claim 28, wherein said measurer includes a HPLC.

30. The diagnostic system of claim 28, wherein said measurer includes a fluorimeter.

31. The diagnostic system of claim 28, wherein said measurer includes an immunochemical assay.

32. A method for determining an efficacy of treatment with an AED (anti-epileptic drug) in a subject, comprising the steps of:

(a) obtaining a sample from the subject;

(b) measuring a concentration of at least two kynurenine metabolites in the sample; and

(c) comparing said concentrations to an expected range of values for individuals with diagnosed epilepsy substantially controlled by treatment with an AED, such that the efficacy of treatment with the AED in the subject is determined.

33. The method of claim 32, wherein step (c) comprises the step of determining a ratio of said at least one neuroprotective metabolite and said at least one neurotoxic metabolite, and the method further comprises the step of:

(d) comparing said ratio to an expected range of values for individuals with diagnosed epilepsy substantially controlled by treatment with an AED, such that the efficacy of treatment with the AED in the subject is determined.

34. The method of claim 32, wherein step (c) comprises the step of determining a ratio of said at least one neuroprotective metabolite and said at least one neurotoxic metabolite, and the method further comprises the step of:

(d) comparing said ratio to a previously determined ratio in the subject, such that the efficacy of treatment with the AED in the subject is determined.

35. The method of claim 34, wherein step (c) is performed after treatment with the AED is stopped.

36. The method of claim 34, wherein step (c) is performed while treatment with the AED is ongoing.

37. The method of claims 33-36, further comprising the steps of:

(e) measuring a concentration of the AED in the plasma sample of the subject; and

(f) correlating said concentration of the AED with said ratio to determine the efficacy of treatment with the AED in the subject.

38. The method of claims 33-36, further comprising the steps of:

(e) determining a dose of the AED; and

(f) correlating said dose of the AED with said ratio to determine the efficacy of treatment with the AED in the subject.

39. The method of claims 37 or 38, further comprising the step of:

(g) adjusting a treatment regimen for the AED in the subject according to the ratios of said metabolites.

40. The method of claim 32, wherein step (c) is performed such that the efficacy of treatment with the AED in the subject is quantitatively determined according to the step of quantitatively comparing said concentrations to said expected range of values.

41. A method for quantitatively diagnosing a predisposition to epilepsy in a subject, the method comprising the steps of:

(a) obtaining a sample from the subject;

(b) measuring a concentration of at least two kynurenine metabolites in the sample, including at least one neurotoxic metabolite and at least one neuroprotective metabolite, to form a pattern and a ratio of said at least two kynurenine metabolites for the subject; and

(c) comparing said pattern and said ratio in the sample to a pattern and a ratio of values of said at least two kynurenine metabolites for individuals with non-treated epilepsy, such that if said ratio and said pattern in the sample is similar to said pattern and said ratio for individuals with non-treated epilepsy, a predisposition to epilepsy is diagnosed in the subject, said predisposition being quantitatively determined according to said ratio.

42. The method of claim 41, wherein the sample is a blood sample.

43. The method of claim 41, wherein said at least two metabolites are selected from the group consisting of TRP (tryptophan), KYN (kynurenine), 3HOKYN (3-hydroxykynurenine), AA (anthranilic acid), 3HOAA (3-hydroxyanthranilic acid), KA (kynurenic acid) and QUIN (quinolinic acid).

44. The method of claim 42, wherein said at least two kynurenine metabolites include at least one neuroprotective metabolite and at least one neurotoxic metabolite.

45. The method of claim 44, wherein said at least two kynurenine metabolites include a pair of metabolites selected from the group consisting of KA and 3HOAA, AA and 3HOAA, and KYN and 3HOKYN.

46. The method of claim 45, wherein a ratio of said concentrations of said pair of metabolites is measured.

47. The method of claim 46, wherein said ratio is selected from the group consisting of KA / 3HOAA, (KA+AA) /3HOAA, KA / QUIN, 3HOAA / 3HOKYN, KA/3HOAAxTRP, (KA+AA)/3HOAAxTRP and KA/(AA + 3HOAA).

48. The method of claim 43, wherein a concentration of each of substantially all of said kynurenine metabolites is measured.

49. The method of claim 43, wherein said concentration of said at least two metabolites is measured by HPLC.

50. A method for evaluating an efficacy of a new AED (anti-epileptic drug) in a subject, comprising the steps of:

(a) obtaining a first sample from the subject;

(b) measuring a first concentration of at least two kynurenine metabolites in the sample;

(c) administering the new AED to the subject;

(d) obtaining a second sample from the subject;

(e) measuring a second concentration of at least two kynurenine metabolites in the sample; and

(f) comparing said first concentration to said second concentration, such that the efficacy of treatment with the new AED in the subject is determined.

51. A composition for controlling epilepsy in a subject, comprising an AED (anti-epileptic drug) for achieving a balance of kynurenine metabolites in the subject, such that an imbalance is corrected.

Add A1

add B1